REMARKS

Reconsideration and allowance are respectfully requested. The title is amended to more accurately reflect the claimed subject matter after the claim are amended as proposed in this response (see Example 41 which describes "immunostimulation").

Claims 1-42, 53-57, 59-63 and 65-69 are pending. The claim amendments are supported by the original disclosure (see page 31, lines 26-27, and page 33, line 6, to page 35, line 2, of the specification). Thus, no new matter has been added.

Entry of the proposed claim amendments is requested to address the Examiner's enablement and written description rejections. Amendment of the claims will reduce the issues on appeal. Furthermore, Applicants submit that the claims as amended herein are consistent with the Examiner's indication of enabled subject matter (see below).

Although the requirements of Rule 97(d) are not satisfied, Applicants bring to the Examiner's attention documents recently submitted in related Appln. No. 09/257,188.

35 U.S.C. 112 – Enablement

Claims 1-42, 53-63 and 65-69 were rejected under Section 112, first paragraph, because it was alleged that the specification does not enable the claims. Applicant traverses.

The Examiner stated on page 2 of the Office Action that the present specification is enabling for "a method for transcutaneous immunization (TCI) comprising applying a formulation that does not include a heterologous adjuvant to intact skin, said formulation consisting of cholera toxin (CT), LT, or *Pseudomonas exotoxin* A (ETA)." In response, Applicants have amended the claims to specify that the formulation is comprised of at least one molecule which is selected from the group consisting of ADP-ribosylating exotoxins, B subunits of ADP-ribosylating exotoxins, and genetically modified ADP-ribosylating exotoxins. In view of the abundance of guidance directed to such molecules and the extensive exemplification provided in the specification, Applicants submit that undue experimentation would not be required to practice the claimed invention. In addition to the ADP-ribosylating exotoxins which the Examiner lists, pertussis toxin (see Examples 13-14), B subunit of cholera toxin (see Examples 37 and 40), and genetically

modified ADP-ribosylating exotoxins like TetC (see Example 31) and LTK63 and LTR72 (see Example 35) are active in transcutaneous immunization. Applicants submit that the fragments of ADP-ribosylating exotoxins like B subunit and TetC are also genetically modified when they are made by recombinant technology.

It is also noted that the molecules recited in claim 1 may act as both antigen and adjuvant (see page 31, lines 11-13, of the specification and original claim 2). Therefore, the negative limitation to the absence of "heterologous adjuvant" in the invention has been removed from the claims as not necessary for their patentability. When transcutaneous immunization or immunostimulation is practiced, any of the recited molecules may act as an adjuvant for a coadministered antigen or a heterologous antigen which is administered at a different site/time.

35 U.S.C. 112 – Written Description

Claim 58 was rejected under Section 112, first paragraph, because it was alleged that Applicants did not have possession of the claimed invention at the time the application was filed. This claim has been canceled to advance prosecution.

Conclusion

Withdrawal of the enablement and written description rejections is requested.

Having fully responded to all of the pending objections and rejections contained in the Office Action (Paper No. 24), Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

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APPENDIX
MARKED-UP VERSION TO SHOW CHANGES

IN THE TITLE

The title is amended as follows.

TRANSCUTANEOUS IMMUNIZATION OR IMMUNOSTIMULATION [WITHOUT HETEROLOGOUS ADJUVANT]

IN THE CLAIMS

The claims are amended as follows.

1. (2 x Amended) A method for transcutaneous immunization or immunostimulation comprising:

(a) providing a formulation comprised of at least one molecule which is an antigen selected from the group consisting of ADP-ribosylating exotoxins, B subunits of ADP-ribosylating exotoxins, and genetically modified ADP-ribosylating exotoxins [derived from a pathogen, wherein said formulation does not include heterologous adjuvant];

(b) applying said formulation epicutaneously to skin of an organism without penetrating said skin's dermis layer; and

(c) inducing an antigen-specific immune response in said organism, wherein at least one epitope of said antigen is recognized.

53. (Amended) A method of claim 1, wherein the antigen is an ADP-ribosylating exotoxin genetically [or chemically] modified to be less toxic to the organism than non-modified ADP-ribosylating exotoxin.

Claim 58 is canceled without prejudice or disclaimer.